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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,396	10/15/2003	A. Raymond Frackelton JR.	3887.1000-001	2101

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EXAMINER	
HUMPHREY, DAVID HAROLD	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 01/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,396	FRACKELTON ET AL.	
	Examiner	Art Unit	
	David Humphrey	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-18 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 7, 10, and 11, drawn to a method for treating a subject afflicted with a proliferative disorder comprising administration to the subject an agent that inhibits the expression of p46 Shc and/or p52 Shc, classified in class 424, subclass 9.2.

II. Claims 2, 10, and 11, drawn to a method for treating a subject afflicted with a proliferative disorder comprising administration to the subject an agent that inhibits the activity of p46 Shc and/or p52 Shc, classified in class 424, subclass 9.1.

III. Claims 3, 8, 9, 10, and 11, drawn to a method for treating a subject afflicted with a proliferative disorder comprising administration to the subject an agent that increases the level of phosphorylated p66 Shc, classified in class 536, subclass 23.1, for example.

IV. Claims 4, 7, and 12, drawn to a method for inhibiting the expression of p46 and/or p52 Shc in a cell, classified in class 536, subclass 24.5.

V. Claims 5 and 12, drawn to a method for inhibiting the activity of p46 and/or p52 Shc in a cell, classified in class 435, subclass 330.

VI. Claims 6, 8, 9, and 12, drawn to a method for increasing the level of phosphorylated p66 Shc in a cell, classified in class 536, subclass 23.1.

VII. Claim 13, drawn to a method for determining whether an agent inhibits the phosphorylation of p46 Shc or p52 Shc, classified in class 436, subclass 86, for example.

VIII. Claim 14, drawn to a method for determining whether an agent inhibits the dephosphorylation of p66 Shc, classified in class 436, subclass 64, for example.

IX. Claim 15, drawn to a method for determining whether an agent inhibits the binding of the Shc A protein to a Shc A binding partner in order to carry out its proliferative function, classified in class 436, subclass 501, for example.

X. Claim 16, drawn to an article of manufacture comprising an agent that inhibits the expression of p46 Shc and/or p52 Shc in a subject, classified in class 536, subclass 24.5.

XI. Claim 17, drawn to an article of manufacture comprising an agent that inhibits the activity of p46 Shc and/or p52 Shc in a subject, classified in class 424, subclass 130.1, for example.

XII. Claim 18, drawn to an article of manufacture comprising an agent that increase the level of phosphorylated p66 Shc in a subject, classified in class 536, subclass 23.1, for example.

2. The inventions are distinct, each from the other because of the following reasons:

The products of Inventions X, XI, and XII are unrelated to the methods of Inventions VII, VIII, and IX. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, agents of Inventions X, XI, and XII are not required to determining whether or not another agent inhibits the phosphorylation of p46 and/or p52 Shc, inhibits the dephosphorylation of p66 Shc, or inhibits the binding of Shc A protein to a binding partner.

The products of Inventions X, XI, and XII, are separate and distinct. Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P § 806.05 for inventive groups that are directed to different products, restriction is deemed proper because these products constitute patentably distinct inventions for the following reasons. Invention X is drawn to an agent that inhibits the expression of p46 and/or p52 Shc. The agent must interfere with steps involved in DNA transcription and or mRNA processing. An agent that interferes with p46 and/or p52 Shc expression is not required for the products of Inventions XI and XII. Invention XI requires an agent that interferes with p46 and/or p52 activity. The agent of Invention XI could therefore be an antibody which upon binding inhibits p46 and/or p52 protein activity or a dominant negative mutant DNA construct of p46 and/or p52 whose expression binds p46 and/or p52 binding partners and thereby reducing the effective concentration and activity of the p46 and/or p52. The agent of Invention XI is not required for Inventions X and XII. The agent of Invention XII increases the level of phosphorylation of p66 Shc. This is not

required for the products of Inventions X and XI. Therefore, the products of Inventions X, XI, and XII are not required one for the other, have different chemical and physical properties, act on different target proteins and DNA molecules, and are therefore patentably distinct.

The methods of Inventions I-IX are separate and distinct. Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: the method have different objectives, method steps and parameters, and utilize different reagents.

For example, Inventions I-III are drawn to methods of treating a subject afflicted with a proliferative disorder. These methods require the use of human subjects which is not required for Inventions IV-IX. Inventions I, II, and III, require the use of patentably distinct reagents. Invention I utilizes an agent that inhibits protein expression of p46 and/or p52 Shc whereas Invention II requires an agent that inhibits protein activity. Invention III requires an agent that increases the phosphorylation of p66 Shc.

Inventions IV-VI have different method objectives. For example, the method objective of Invention IV is to inhibit p46 and/or p52 expression in a cell whereas the method of Invention V is to inhibit p46 and/or p52 protein activity in a cell. These are separate and distinct from the objective of Invention VI which is to increase the level of phosphorylated Shc in a cell.

Inventions VII-IX are drawn to methods of screening agents for patentably distinct purposes. For example, Invention VII is a method of screening for an agent that inhibits the phosphorylation of p46 and/or p52 Shc. Invention VIII is a method of screening for an agent that inhibits the dephosphorylation of p66 Shc whereas Invention IX is a method of screening for an agent that inhibits the binding of a Shc A protein to a Shc A binding partner. Since Inventions VII-IX involve screening for agents with separate and distinct functions, the Inventions are patentably distinct.

Inventions X and I, X and IV, XI and II, XI and V, XII and III, XII and VI, are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product of Invention X, such as a ribozyme, can be used in another, materially different process such as an in vitro translation system. The product of Invention XI, such as an antibody, can be used to purify the target antigen. The product of Invention XII, such as a p66 Shc-encoding expression vector, can be used to make and purify p66 Shc for in vitro binding assays.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance,

whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. This application contains claims directed to the following patentably distinct species of the claimed invention: claims 11 and 12 contain proliferative diseases selected from the group of

a. prostate cancer

b. ovarian cancer

c. breast cancer

Prostate, ovarian, and breast cancer are patentably distinct since they involve separate and distinct tissues, patient populations, different diagnostic symptoms and tests, and separate methods of treatment. For example, prostate cancer occurs in men with symptoms such as frequent urination, painful or burning urination, weak or interrupted flow of urine, blood in urine or semen, and pain ejaculation. Breast cancer occurs predominantly in women with symptoms such as a lump or thickening in or near the breast or in the underarm area, a change in the size or shape of the breast and a discharge from the nipple. In contrast, ovarian cancer is associated with symptoms such as abdominal/pelvic pain, vaginal bleeding, bloating, abdominal distension, irregular menses, and change in bowel habit. Therefore, the species prostate cancer, breast cancer and ovarian cancer are patentably distinct and a search of all would require an undue search burden on the USPTO's resources.

If Applicant elects Invention I, II, III, IV, V, or VI, Applicant is required under 35 U.S.C. 121 to further elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 11 and 12 are generic.

5. This application contains claims directed to the following patentably distinct species of the claimed invention: claim 7 contains agents selected form the group of:

a. siRNA

b. ribozyme

c. DNAzyme

siRNA, ribozymes and DNAzymes are structurally and functionally distinct. For example, issues of concern when working with siRNA such as moderate to low G/C content 36-52%, low internal stability of the sense 3'end, at least one A/T duplex between position 15-19, lack of internal repeats and a Tm < 60 °C are not concerns when working with ribozymes or DNAzymes. Ribozymes such as the "hammerhead" ribozyme and the "hairpin" ribozyme can cleave GUC sites, but the hammerhead can also cleave at GUA, GUU, CUC and UUC with comparable efficiency [4] and sometimes at AUC. These properties and functions are not required for either siRNA or DNAzymes. DNAzymes are single stranded DNA that have catalytic function which is not required for ribozymes or siRNA. Therefore, the species of siRNA, ribozyme, and DNAzyme are patentably distinct and would require an undue search burden on the USPTO's resources.

If Applicant elects Invention I or IV, Applicant is required under 35 U.S.C. 121 to further elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claim 7 is generic.

6. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Humphrey whose telephone number is (571) 272-5544. The examiner can normally be reached on Mon-Fri 8:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Humphrey, Ph.D.

January 11, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER